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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,051	08/08/2006	Kohichi Tanaka	023312-0118	5841

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EXAMINER	
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ART UNIT	PAPER NUMBER
1633	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/553,051	TANAKA ET AL.	
	Examiner	Art Unit	
	FEREYDOUN G. SAJJADI	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2 and 5-14* is/are pending in the application.

4a) Of the above claim(s) *8-10 and 12-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,5-7 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/20/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission and amendment filed on November 20, 2008, that includes a response to the office action dated June 20, 2008, have been entered. Claims 2 and 5-14 are pending in the application. Claims 2, 5 and 11 have been amended. No claims were cancelled or newly added. Claims 8-10 and 12-14 stand withdrawn from further consideration, with traverse. Applicants should note that claim 11 has been presented with the incorrect status identifier of withdrawn, that is not compliant with 37CFR § 1.121 (c). While Applicants may cancel claims, there is no provision for Applicants withdrawing examined claims during prosecution. Accordingly, claims 2, 5-7 and 11 are under current examination.

Information Disclosure Statement

The information disclosure statement filed November 20, 2008 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been fully considered, as document A8 by Nike is in the Japanese language. Further, there is no indication that the document was described in the European Search Report dated August 21, 2007, as alleged by Applicants.

Response & Withdrawn Claim Rejections - 35 USC § 112- Second Paragraph

Claim 5 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite, in the previous office action dated June 20, 2008. Applicants' claim amendment deleting the indefinite language obviates the ground of rejection. Thus, the rejection is hereby withdrawn.

Claim 11 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite, in the previous office action dated June 20, 2008. Applicants have correctly identified the claim as a product by process claim. Thus, the rejection is hereby withdrawn.

Response & Withdrawn Claim Rejections - 35 USC § 103

Claims 2, 5-7 and 11 were rejected under 35 U.S.C. §103(a) as being unpatentable over Watase et al. (Eur. J. Neurosci. 10:976-988; 1998), in view of Chitnis et al. (J. Clin. Invest. 108(5):739-747; 2001). Applicants have provided a Declaration by co-inventor Kohichi Tanaka, under 37 CFR §1.132, describing the surprising phenotypic differences observed as result of backcrossing for ten times, transgenic GLAST knockout mice with 129sv and C57BL/6J mice respectively, to obtain inbred GLAST knockout mouse having less genotypic and phenotypic background variation, but also, having an intraocular pressure within a normal range (not greater than 21 mmHg) and 20% - 50% less retinal ganglions cells than a wild-type mouse, only in the C57BL/6J genotypic background. As no observable reduction in the number of retinal ganglion cells was found in a GLAST knockout mouse obtained by backcrossing with the 129sv strain, compared to a wild type mouse, it is clear that the combination of the cited prior art references would not have predicted the instantly claimed phenotype for the knockout mice. Thus, the rejection is hereby withdrawn. Applicants' arguments are moot in view of the withdrawn rejection.

New Claim Rejections - 35 USC § 112-Scope of Enablement

Claims 2, 5-7 and 11 are newly rejected under 35 U.S.C.§112, first paragraph, because the specification, while being enabling for a GLAST knockout mouse deficient in the function of an endogenous GLAST gene, wherein the genome of said mouse, except for the targeted

endogenous GLAST gene, is the same as that of a C57BL/6 strain mouse, and wherein when ischemic load is not applied, the intraocular pressure is not greater than 21mmHg, and the number of cells in the retinal ganglion is 20% to 50% less than that of a wild-type mouse; does not reasonably provide an enablement for a GLAST knockout mouse, having normal intraocular pressure and 20% to 50% less retinal ganglion cells than a wild-type mouse, in any genetic background, or a genetic background that is closer to a C57BL/6 strain, as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection is based on the absence of an enabling disclosure for a transgenic GLAST knockout mouse whose genetic background is not C57BL/6 and wherein when ischemic load is not applied, the intraocular pressure is not greater than 21mmHg, and the number of cells in the retinal ganglion is 20% to 50% less than that of a wild-type mouse. In determining whether Applicant's claims are enabled, it must be found that one of skill in the art at the time of invention by Applicant would not have had to perform "undue experimentation" to make and/or use the invention claimed. Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404:

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

MPEP § 2164.04 states: "[W]hile the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection."

When given their broadest reasonable interpretation, in view of the as filed specification, base claim1 encompasses a transgenic GLAST knockout mouse deficient in the function of an endogenous GLAST gene, wherein the genetic background of said knockout mouse remains undefined; and claim 11encompasses said transgenic mouse whose genetic background is closer

to the C57BL/6 strain mouse. Thus, neither claim indicates that the genetic background of the mice is the same as the genetic background of a C57BL/6 strain mouse.

The state of the prior art is effectively summarized by the reference of Watase et al. (Eur. J. Neurosci. 10:976-988; 1998), teaching the inactivation of the endogenous mouse GLAST gene (Abstract) in ES cells, the generation of chimeric mice by injecting targeted ES cells into C57BL/6 blastocysts and germline transmission of the targeted mutation in the GLAST gene to generate homozygous and heterozygous mutants (first column, p. 978). Watase et al. however did not describe the instantly claimed phenotype in their transgenic offspring.

The prior art had additionally taught that the genetic background of transgenic mice could affect the resulting phenotype following a gene knockout. To ensure a uniform genetic background the prior art generally teaches routine backcrossing to the desired strain for at least ten generations. For example, Chitnis et al. (J. Clin. Invest. 108(5):739-747; 2001) describe the effect of targeted disruption of mouse STAT genes in knockout mice (Abstract), and the backcross of their knockout mice onto a C57BL/6 background for at least ten generations (first column, p. 740).

Applicants' published specification teaches backcrossing at least 9 times and more preferably at least 15 times (paragraph [0077]), while being silent on the claimed phenotype being observed in any background other than C57BL/6. Further, the 37 CFR 1.132 Declaration by co-inventor Tanaka describes backcrossing of the GLAST knockout mouse for ten times to two different strains that included C57BL/6, and observing the claimed phenotype only in the C57BL/6 background. However, claim 11 recites crossing a total of 5 times to bring the genetic background closer to the C57BL/6 strain mouse, to produce a transgenic mouse with the instantly claimed phenotype.

Therefore, a person of skill in the art would not know absent further experimentation how close the genetic background of the GLAST knockout mice would have to get to that of a C57BL/6 strain mouse to achieve the claimed phenotype. The skilled artisan would further not know whether any genetic background would result in the claimed phenotype, as in claim 1. As the required experimentation would not predictably show the instantly claimed phenotype, it the further experimentation would be considered undue.

Therefore, in light of the guidance provided by the disclosure of the application and the absence of any teaching in the prior art regarding the instantly claimed phenotype of GLAST knockout mice, it would require undue experimentation by the skilled Artisan to obtain GLAST knockout mice displaying an intraocular pressure that is not greater than 21mmHg and the number of cells in the retinal ganglion reduced by 20% to 50% when ischemic load is not applied, in any genetic background, or a genetic background closer to C57BL/6. Hence, absent a strong showing by Applicant, in the way of specific guidance and direction, and/or working examples demonstrating the same, such invention as claimed by Applicant is not enabled.

Please note that the ground of rejection for claim 1 may be obviated by incorporating the limitation of claim 5 into base claim 1 as set forth in the enabled scope above.

Conclusion

Claims 2, 5-7 and 11 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to FEREYDOUN G. SAJJADI whose telephone number is (571)272-3311. The examiner can normally be reached on 6:30 AM-3:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Fereydoun G Sajjadi/
Examiner, Art Unit 1633